

WHAT IS CLAIMED IS:

Sub C1

1. Purified urate oxidase (uricase) substantially free of aggregates larger than octamers.
2. The uricase of Claim 1, wherein the uricase is mammalian uricase
- 5 3. The uricase of Claim 2, wherein the uricase is porcine liver, bovine liver or ovine liver uricase.

Sub B2

4. The uricase of Claim 1, wherein the uricase is recombinant.
5. The uricase of Claim 4, wherein the uricase has substantially the sequence of porcine, bovine, ovine or baboon liver uricase.
- 10 6. The uricase of Claim 4, wherein the uricase is chimeric.
7. The uricase of Claim 6, wherein the chimeric uricase contains portions of porcine liver and baboon liver uricase.

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8. The uricase of Claim 7, wherein the chimeric uricase is PKS uricase.
- 15 9. The uricase of Claim 4, wherein the uricase has substantially the sequence of baboon liver uricase in which tyrosine 97 has been replaced by histidine.
10. The uricase of Claim 4, wherein the uricase comprises an amino terminal and a carboxy terminus, and wherein the uricase is truncated at one terminus or both termini.

- 20 11. The uricase of Claim 1, wherein the uricase is a fungal or microbial uricase.

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12. The uricase of Claim 11, wherein the fungal or microbial uricase is isolated from *Aspergillus flavus*, *Arthrobacter globiformis*, *Bacillus sp.* or *Candida utilis*, or is a recombinant enzyme having substantially the sequence of one of said uricases.

- 25 13. The uricase of Claim 1, wherein the uricase is an invertebrate uricase.

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14. The uricase of Claim 13, wherein the invertebrate uricase is isolated from *Drosophila melanogaster* or *Drosophila pseudoobscura*, or is a recombinant enzyme having substantially the sequence of one of said uricases.

15. The uricase of Claim 1, wherein the uricase is a plant uricase.

16. The uricase of Claim 15, wherein the plant uricase is isolated from root nodules of *Glycine max* or is a recombinant enzyme having substantially the sequence of said uricase.

17. The uricase of Claim 1 conjugated to poly(ethylene glycol) or poly(ethylene oxide), wherein the uricase in said conjugate is substantially free of aggregates larger than octamers.

18. The uricase conjugate of Claim 17, wherein said poly(ethylene glycol) is monomethoxy poly(ethylene glycol).

19. The uricase of Claim 17, wherein said uricase is conjugated to said poly(ethylene glycol) or poly(ethylene oxide) via a linkage selected from the group consisting of urethane (carbamate), secondary amine and amide.

20. The uricase conjugate of Claim 17, wherein said poly(ethylene glycol) or poly(ethylene oxide) has a molecular weight between about 5 kDa and 30 kDa.

21. The uricase conjugate of Claim 20, wherein said poly(ethylene glycol) or poly(ethylene oxide) has a molecular weight between about 10 kDa and 20 kDa.

22. The uricase conjugate of Claim 17, wherein the average number of strands of said poly(ethylene glycol) or poly(ethylene oxide) strands is between about 2 and 12 per uricase subunit.

23. The uricase conjugate of Claim 22, wherein the average number of strands of said poly(ethylene glycol) or poly(ethylene oxide) strands is between about 6 and 10 per uricase subunit.

24. The uricase conjugate of Claim 23, wherein the average number of strands of said poly(ethylene glycol) or poly(ethylene oxide) is between about 7 and 9 per uricase subunit.

25. The uricase conjugate of Claim 17, wherein the poly(ethylene glycol) or poly(ethylene oxide) is linear.

26. The uricase conjugate of Claim 17, wherein the poly(ethylene glycol) or poly(ethylene oxide) is branched.

27. A pharmaceutical composition for lowering uric acid levels in a body fluid or tissue, comprising the conjugate of Claim 17 and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of Claim 27, wherein said composition is stabilized by lyophilization and dissolves upon reconstitution to provide solutions suitable for parenteral administration.

5 ~~29.~~ A method for purifying uricase having reduced immunogenicity, comprising the step of separating uricase aggregates larger than octamers in uricase fractions, and excluding such aggregates from the purified uricase.

30. The method of Claim 29, wherein said separating step is selected from the group consisting of ion-exchange chromatography, size-exclusion chromatography and ultrafiltration.

10 31. The method of Claim 30, wherein said separating step comprises the step of detecting aggregates larger than octamers in uricase fractions and excluding said fractions containing said aggregates.

32. The method of Claim 31, wherein said detecting step comprises measurement of light scattering.

Sub B8
33. Isolated uricase prepared by the method of Claim 29.

Add B1

add C3

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